# Functional genomic screening in drug discovery

Functional genomic screens enable modulation of hundreds or thousands of genes in a single experiment to identify genetic pathways, cellular processes, novel therapeutic targets, and to genetically profile existing or potential therapeutics.

**BASIC REASEARCH**
Understanding the Genetic Impact of the Disease

**TARGET DISCOVERY**
Identifying and Validating Disease-Relevant Targets

**LEAD IDENTIFICATION**
Screening Promising Leads Faster

**LEAD OPTIMIZATION**
Maximizing Selectivity and Potency of Compounds

Gene expression can be regulated using either RNAi or CRISPR technology, where RNAi represses gene expression at the mRNA level (knockdown), while CRISPR works at the DNA level and can permanently knockout or modulate genes. The two CRISPR screening approaches are:

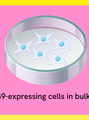
## POOLED

**Pooled CRISPR Screening:** Editing is performed with a mixture of RNA (gRNA), producing a high number of perturbations.

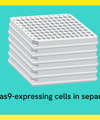
## ARRAYED

**Arrayed CRISPR Screening:** Perturbation occurs in a single well for clear phenotype to genotype correlation.

### MODEL PREPARATION

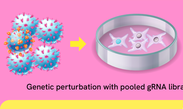


CAS9-expressing cells in bulk

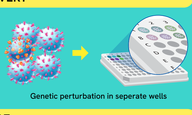


Cas9-expressing cells in separate wells

### LIBRARY DELIVERY

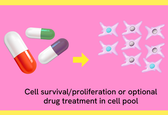


Genetic perturbation with pooled gRNA library



Genetic perturbation in seperate wells

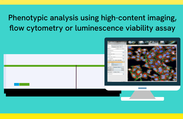
### CHALLENGE



Cell survival/proliferation or optional drug treatment in cell pool

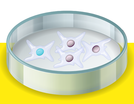
Cell survival/proliferation or optional drug treatment in seperate wells

### READ-OUT


| | POOLED SCREENING | ARRAYED SCREENING |
|---|---|---|
| **Advantages** | • Less expensive<br>• Large number of genes can be integrated at once<br>• Suitable for longer *in vivo* studies<br>• No specialized/automated equipment needed | • Multi-parametric read-outs<br>• Suitable for more complex cell models<br>• More choices in reagent formats, including non-viral transfection and cherry-picking options<br>• Clear phenotype to genotype correlation<br>• Improved editing efficiency by targeting the same gene with several gRNAs in one well |
| **Disadvantages** | • Only simple read-outs: cell death or survival, reporter gene and sortable biomarkers<br>• An edited cell type can influence other cells in the mixed population negatively<br>• Very large cell population needed at start and to be maintained in large flasks | • Lab automation equipment needed<br>• Assays often suffer from low transfection/electroporation efficiencies |

## Read-out methods



### POOLED SCREENING

- NGS At Different Time Points or After Different Selective Pressures
- NGS Combined with Certain Biological Characteristics by FACS Sorting Using Reporter Gene Or Surface Biomarker
- scRNA Sequencing linking gRNA Expression with Transcriptomic Profile
- In-Situ Sequencing linking gRNA Expression with Imaging Phenotype

### ARRAYED SCREENING

- Fluorescence or luminescence detection to analyse Cell Viability and Proliferation
- Imaging - Cell Morphology, Biomarker Expression and Localization
- Live Cell Imaging – Differentiation, Migration
- Proteomic and Metabolomic Profiling

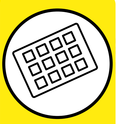
## Products

### Gene editing & modulation reagents

- CRISPR
- RNAi

### Cell analysis

- High-content imaging
- Cell counters
- Live cell imaging
- Imaging reagents
- Image analysis software



### Detection

- Viability assays
- Immunoassays
- Reporter gene assays
- Microplate readers

### Sequencing based read-out

- Single cell RNA sequencing reagents
- Antibodies for selection
- Single cell sample storage & processing

## Functional genomic screening services

Comprehensive solutions to perform pooled and arrayed screens for you with our CRISPR knockout, CRISPR activation, CRISPR inhibition, and dual CRISPRa/i screening platforms.

**LEARN MORE**

https://www.revvity.com/

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